Case Report

Vitiligo Appearing after Oral Isotretinoin Therapy for Acne

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Isotretinoin is an effective treatment for severe and scarring acne. In this report, we describe a case developing vitiligo after isotretinoin therapy for scarring acne. It is not known whether this was a coincidence or might be precipitated by the treatment.

1. Introduction

Isotretinoin is an effective therapy for severe acne. It has the best influence on the health-related quality of life in acne patients [1]. Some side effects of isotretinoin are well known and predictable such as cheilitis and xerosis. Other side effects are known but less common such as hyperlipidemia. It is a known teratogenic medication and is contraindicated in pregnancy. Several other side effects are reported but less commonly [2]. Depressive symptoms and suicidal ideation are other issues for the use of isotretinoin [3].

Vitiligo is an autoimmune disease of the skin and is thought to be of multifactorial causation [4, 5]. Vitiligo patients have high prevalence of other autoimmune diseases [6]. Thyroid function tests and thyroid autoantibodies might be used for screening for vitiligo patients [7].

Here we report a case of vitiligo appearing after isotretinoin therapy. It is unknown whether this was a side effect of oral isotretinoin therapy or a coincidence.

2. Case Presentation

A 21-year-old female presented to the dermatology clinic with severe facial acne with some scars. Severity of acne was graded as 4 on IGA scale (investigator global assessment of acne) which is accepted by American FDA [8]. She has used topical treatments including topical retinoids (Tretinoin and Adapalene creams) for several months with no satisfactory results. On presentation, she did not have any other complaints and was not on any systemic treatments. Her weight was 45 kg.

After initial laboratory works (lipid profile and liver enzymes) which were in the normal range, she was started on 20 mg isotretinoin. She was maintained on 20 mg (0.5 mg/kg) for 6 months. She had mild cheilitis and skin dryness and complained of mild hair fall. Repeated liver enzymes and lipid profile after one month and 4 months were within normal range. Her acne has cleared completely.

She stopped the treatment because of inability to attend the clinic for few weeks.

After 2 months of stopping isotretinoin, she noticed a single whitish patch on her nose. She is fair-skinned, so the lesions were not apparent except on tanning after sun exposure. Antifungal treatment was used for few weeks topically with no improvement as it was thought to be pityriasis versicolor. Then the lesion began to expand, and new lesions appeared around mouth, cheeks, and right ankle area. Hand lesions appeared as well (Figure 1). On Wood's light examination, the patches were revealed to be depigmented. The pattern of acrofacial vitiligo is noted [5].

Thyroid function test initially showed low TSH, 0.177 uIU/L (normal range: 0.27-4.2), and normal levels of free T3, 6.11 pmol/L (2.8- 7), and free T4, 15.7 pmol/L (12-22). Three months later, TSH was high, 9.61 uIU, and normal free T3 (4.7 pmol/L) and free T4 (12.2 pmol/L) and thyroid antibodies were positive; thyroid peroxidase antibodies were 157.59 IU/mL (normal range: 0-5.6) and thyroid thyroglobulin antibodies were 66.09 IU/mL (normal range: 0-4.11). She was started on thyroxine and followed up at the medical clinic. Vitamin D3 was low, 47.11 nmol/L (normal range: 75-250 nmol/L), and she was started on vitamin D supplement as well. She had no family history of vitiligo. There was

FIGURE 1: Vitiligo lesions in the hands.

a family history of diabetes, hypertension, and systemic lupus erythematosus (SLE) and her auntie died from renal complication of SLE.

She was started on Tacrolimus 0.1% cream. Mild improvement was noted in some of lesions after 8 weeks. New lesions appeared again after another month. She stopped the topical treatment and opted to homeopathic treatment.

3. Discussion

In this report, we describe a case of vitiligo appearing for the first time after using oral isotretinoin for scarring acne. The most common side effects with oral isotretinoin therapy are skin dryness and cheilitis. In a study of 1743 cases reviewing the side effects of isotretinoin, cheilitis was reported to be the most common side effect followed by eczema and tiredness [9]. Of note, vitiligo was not reported in this study. Some rare complications have been reported like acute myocardial infarction linked with the increase in lipids [10], inflammatory bowel disease [11], and severe myopathy [12].

Vitiligo was reported around lips in a patient treated with isotretinoin owing to the cheilitis as a Koebner phenomenon. This patient suffered from vitiligo prior to the initiation of isotretinoin [13]. Our case is different as she developed vitiligo lesions for the first time after isotretinoin therapy. One patient out of 50 developed vitiligo while on low-dose (20 mg/day for 3 months) isotretinoin therapy for acne [14], while larger-scale studies did not report vitiligo as a side effect (150 patients) [15].

Vitiligo is a multifactorial polygenic with incomplete penetrance inherited disease with a significant environmental influence. Autoimmune diseases, especially thyroid diseases, are very common association with vitiligo [16]. In vitro studies have shown that retinoids may have a proapoptotic effect on melanocytes [17]. Melanocytes express some retinoid receptors that are lost in melanoma compared to benign nevi [18], which could be a direct cause of vitiligo in this case. Additionally, retinoids might increase inflammatory cytokines via mast cells [19]. In this case, it is unknown whether oral isotretinoin acted here as a trigger to induce the disease via one of the pathways in a susceptible individual or it

was a mere coincidence. Reporting similar cases if happening can help identify whether this is a true side effect of the medication.

Conflicts of Interest

The author declares that there are no conflicts of interest.

References

- [1] P. Chernyshov, L. Tomas-Aragones, L. Manolache et al., "Which acne treatment has the best influence on health-related quality of life? Literature review by the European Academy of Dermatology and Venereology Task Force on Quality of Life and Patient Oriented Outcomes," *Journal of the European Academy of Dermatology and Venereology*.
- [2] P. Brzezinski, K. Borowska, A. Chiriac, and J. Smigielski, "Adverse effects of isotretinoin: A large, retrospective review," *Dermatologic Therapy*, vol. 30, no. 4, p. e12483, 2017.
- [3] J. M. Oliveira, G. Sobreira, J. Velosa, D. Telles Correia, and P. Filipe, "Association of Isotretinoin With Depression and Suicide: A Review of Current Literature," *Journal of Cutaneous Medicine and Surgery*, vol. 22, no. 1, pp. 58–64, 2018.
- [4] A. Alikhan, L. M. Felsten, M. Daly, and V. Petronic-Rosic, "Vitiligo: a comprehensive overview Part I. Introduction, epidemiology, quality of life, diagnosis, differential diagnosis, associations, histopathology, etiology, and work-up," *Journal of the American Academy of Dermatology*, vol. 65, no. 3, pp. 473–491, 2011.
- [5] M. Rodrigues, K. Ezzedine, I. Hamzavi, A. G. Pandya, and J. E. Harris, "New discoveries in the pathogenesis and classification of vitiligo," *Journal of the American Academy of Dermatology*, vol. 77, no. 1, pp. 1–13, 2017.
- [6] L. Gill, A. Zarbo, P. Isedeh, G. Jacobsen, H. W. Lim, and I. Hamzavi, "Comorbid autoimmune diseases in patients with vitiligo: A cross-sectional study," *Journal of the American Academy of Dermatology*, vol. 74, no. 2, pp. 295–302, 2016.
- [7] M. Liu, E. Murphy, and E. H. Amerson, "Rethinking screening for thyroid autoimmunity in vitiligo," *Journal of the American Academy of Dermatology*, vol. 75, no. 6, pp. 1278–1280, 2016.
- [8] R. Carruthers, "Acne Vulgaris," *Drugs*, vol. 8, no. 3, pp. 217–223, 1974.

- [9] M. Rademaker, "Adverse effects of isotretinoin: A retrospective review of 1743 patients started on isotretinoin," *Australasian Journal of Dermatology*, vol. 51, no. 4, pp. 248–253, 2010.
- [10] N. Lorenzo, P. Antuña, L. Dominguez, F. Rivero, T. Bastante, and F. Alfonso, "Acute myocardial infarction in a young woman on isotretinoin treatment," *International Journal of Cardiology*, vol. 181, pp. 39–41, 2015.
- [11] S. AlBreiki, I. Bukhari, and H. Bosbait, "Case report: inflammatory bowel disease and isotretinoin: An overlooked potential side effect?" *Journal of the Saudi Society of Dermatology Dermatologic Surgery*, vol. 16, pp. 73–75, 2012.
- [12] F. Sameem and Semira, "Isotretinoin-induced acute severe myopathy involving pelvic girdle muscles: A case report," *Indian Journal of Pharmacology*, vol. 48, no. 5, pp. 601–603, 2016.
- [13] M. L. Garner, D. B. McShane, C. N. Burkhart, and D. S. Morrell, "Isotretinoin and vitiligo: Can chronic cheilitis cause koebnerization?" *Pediatric Dermatology*, vol. 32, no. 3, pp. e108–e109, 2015.
- [14] P. K. Rao, R. M. Bhat, B. Nandakishore, S. Dandakeri, J. Martis, and G. H. Kamath, "Safety and efficacy of low-dose isotretinoin in the treatment of moderate to severe acne vulgaris," *Indian Journal of Dermatology*, vol. 59, no. 3, p. 316, 2014.
- [15] M. D. F. D. M. Brito, I. P. Sant'Anna, J. C. S. Galindo, L. H. P. D. M. Rosendo, and J. B. Dos Santos, "Evaluation of clinical adverse effects and laboratory alterations in patients with acne vulgaris treated with oral isotretinoin," *Anais Brasileiros de Dermatologia*, vol. 85, no. 3, pp. 331–336, 2010.
- [16] B. W. Lee, R. A. Schwartz, J. Hercogová, Y. Valle, and T. M. Lotti, "Vitiligo road map," *Dermatologic Therapy*, vol. 25, no. 1, pp. S44–S56, 2012.
- [17] I. Baldea, G.-E. Costin, Y. Shellman et al., "Biphasic pro-melanogenic and pro-apoptotic effects of all-trans-retinoic acid (ATRA) on human melanocytes: Time-course study," *Journal of Dermatological Science*, vol. 72, no. 2, pp. 168–176, 2013.
- [18] S. Hyter and A. K. Indra, "Nuclear hormone receptor functions in keratinocyte and melanocyte homeostasis, epidermal carcinogenesis and melanomagenesis," *FEBS Letters*, vol. 587, no. 6, pp. 529–541, 2013.
- [19] M. Babina, S. Guhl, E. Motakis et al., "Retinoic acid potentiates inflammatory cytokines in human mast cells: Identification of mast cells as prominent constituents of the skin retinoid network," *Molecular and Cellular Endocrinology*, vol. 406, pp. 49–59, 2015.